1. Abstract

Title

Drug utilisation study (DUS) on flupirtine-containing products

Retrospective drug utilisation study using patient-level databases to characterise prescribing practices of flupirtine-containing drugs during routine clinical use and assess the main reasons for prescription by representative groups of prescribers

Version: 11.11.2016

Keywords

Drug utilisation study, flupirtine, prescribing practice, effect of RMM

Rationale and background

In September 2013 PRAC/EMA had restricted the use of flupirtine to acute pain with a maximum treatment duration of 14 days following safety concerns due to hepatotoxicity reactions during long term use and further consideration of the current evidence for the flupirtine efficacy. The implementation of RMM for flupirtine-containing products was started in July 2013 with the distribution of DHPC, followed by the change of SmPC in September 2013 and finalised with the distribution of the educational material in February 2015.

Research question and objectives

The aim of the study was to characterise prescribing practices for flupirtine-containing medicinal products during routine clinical use and assess main reasons for prescription by representative groups of prescribers in Germany before and after the implementation of RMM for flupirtine-containing medicinal products.

Study design

This study employed a retrospective cohort analysis with pre-post design based on secondary data use from two of longitudinal databases in Germany.

Setting

The study was conducted in the outpatient setting in Germany.

The following three periods were considered for the final report:

- Reference period (before referral and implementation of RMM): 01.01.2012 – 31.12.2012
- Assessment period I (after change of SmPC and distribution of DHPC): 01.01.2014 – 31.12.2014
- Assessment period II (after change of SmPC, distribution of DHPC and distribution of the educational material in Germany): 01.04.2015 – 31.03.2016

Subjects and study size, including dropouts

All patients who have received at least one prescription for flupirtine –containing products in the reference period or in the assessment periods I or II and fulfilled the inclusion criteria were considered in the analysis. A total of 46,273 patients from IMS® Disease Analyzer and 558,693 patients from IMS® LRx were included for the final analysis.

Variables and data sources

Two German longitudinal patient-level databases were used as data sources for the flupirtine utilization study (the EMR database IMS® Disease Analyzer and the prescription database IMS® LRx).

The variables for analysis included characteristics of patients and prescribing physicians, patients' medical history, prescription information for flupirtine (pack size, number of packages, formulation, strength), indication, concomitant use of hepatotoxic drugs, liver function monitoring.

Results

IMS® Disease Analyzer

In total, 18,291 flupirtine users in the reference period (2012), 15,982 in the assessment period I (2014) and 12,000 in the assessment period II (April 2015 to March 2016) were included in the analysis. The patient number decreased by 12.6% and by 34.4% between reference period and assessment periods I and II, respectively.

Proportion of patients without history of liver diseases or alcohol abuse was similar in three study periods (88.0%, 87.6% and 87.4%); conditions contraindicated with use of other analgesics (diagnoses or long-term medication for these conditions) were identified for 69.4% in 2012 and increased significantly to 72.7% in the assessment period I (p-value 0.0001) and not statistically significantly to 71.4% in the assessment period II (p-value 0.2232). Pre-treatment with other analgesics (within 12 months pre-index) was found in 53.0% of patients in the reference period, 51.7% in the assessment period I and in 51.2% of patients in the assessment period II. The overall proportion of flupirtine prescriptions for diagnoses associated with acute pain (acute pain episodes, exacerbations) was 71.0% in the reference period, 72.4% in the assessment period I (p-value <0.0001) and 71.5% in the assessment period II (p-value vs. reference period 0.2454). Proportion of prescriptions with duration ≤14 days increased significantly by 9.8% (from 75.1% in the reference period to 84.9% in the assessment period I; p-value <0.0001) and by 15.5% (from 75.1% in the reference period to 90.6% in the assessment period II; p-value <0.0001). Proportion of patients with short-term treatment episodes up to 14 days increased by 11.4% (from 74.8% in the reference period to 86.2% in the assessment period I; p-value <0.0001) and by 16.5% (from 74.8% in 2012 to 91.3% in the assessment period II; p-value <0.0001). The proportion of flupirtine prescriptions without concomitant use of drugs known to have potential hepatotoxic effect was similar in three study periods with 71.8%, 72.5% and 71.8% (difference between assessment periods and reference period not statistically significant). Proportion of prescriptions with liver function monitoring during one month after prescription date increased slightly from 10.1% (2012) to 11.0% (2014) and 12.6% (April 2015 - March 2016).

IMS® LRx

In total, 248,738 flupirtine users in the reference period, 163,191 in the assessment period I and 146,764 in the assessment period II were included in the analysis. The patient number

decreased by 34.4% and by 41.0% between reference period and assessment periods I and II, respectively.

Overall, the results based on IMS® LRx were in line with those from the IMS® Disease Analyzer. However, the increase in the proportion of patients with short-term treatment episodes up to 14 days was with 18.7% (from 67.9% to 86.6%; p-value <0.0001) between reference and assessment period I and with 22.7% (from 67.9% to 90.6%; p-value <0.0001) between reference and assessment period II more prominent.

Discussion

The results of the final analysis are in line with the results of the interim analysis and show that the implementation of RMM (distribution of DHPC, change of SmPC, distribution of educational material) was effective and resulted in change in prescribing behaviour of physicians in Germany. This is particularly supported by the considerable increase of short-term use (≤ 14 days). The overall reduction of prescriptions indicates that the physicians consider the change in the SmPC in clinical practice and restrict flupirtine prescriptions to the targeted patient population.

Marketing Authorisation Holder(s)

According to Annex 3 of the RMP (see Annex 3)

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